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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/691,506	10/24/2003	Hirohiko Tsuzuki	Q77914	2041

7590 07/18/2005
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EXAMINER

SINGH, SATYENDRA K

ART UNIT PAPER NUMBER

1651

DATE MAILED: 07/18/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

10/691,506

Applicant(s)

TSUZUKI ET AL.

Examiner

Satyendra K. Singh

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 13 June 2005.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-18 is/are pending in the application.
- 4a) Of the above claim(s) 6-18 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-5 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 24 October 2003 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All b) ☐ Some * c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
 - ☐ Certified copies of the priority documents have been received in Application No. _____.
 - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- ☒ Notice of References Cited (PTO-892)
- ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date _____
- ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date _____
- ☐ Notice of Informal Patent Application (PTO-152)
- ☐ Other: _____

DETAILED ACTION

Applicant's election of group I, claims 1-5 in the response filed with the office on 06/13/2005 is duly acknowledged.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-4 are rejected under 35 U.S.C. 102(b) as being anticipated by Skjak-Braek et al (a WIPO document, WO 91/09119, [N]).

Claim 1 is drawn to "a carrier for cell culture comprising a **water-containing polymer gel** containing **chitosan**, wherein the water-containing polymer gel is **coated with collagen and/or alginic acid**" which is anticipated by prior art [N].

Prior art [N] teaches microcapsules for encapsulating cells comprising hydrogel such as alginate (see prior art, page 8-10, and drawings, in particular) containing chitosan (see prior art, page 9, lines 14-19, in particular), wherein the water-containing polymer gel is coated with alginate (see prior art, page 9, lines 9-13, in particular).

Claim 2 is drawn to "the carrier for cell culture according to claim 1, which comprises **two or more coated layers**" which is anticipated by the prior art [N].

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Prior art teaches a microcapsule for encapsulating cells comprising a water-containing polymer gel containing chitosan, wherein the polymer gel is coated with alginic acid, and further which comprises two or more coated layers such as an additional layer of hyaluronic acid on top of the cationic layer made of poly-L-lysine or chitosan (see prior art, page 8, lines 28-32, and page 9, lines 4-19, in particular).

Claim 3 and 4 are drawn to "the carrier for cell culture according to claim 2, wherein an **outermost layer** is a **collagen-coating** layer or an **alginic acid-coating** layer; and wherein an outermost layer is an alginic acid-coating layer" which is anticipated by prior art [N].

Prior art teaches a microcapsule for encapsulating cells comprising a water-containing polymer gel containing chitosan, wherein the polymer gel is coated with alginic acid, comprises of two or more coated layers; and wherein the outermost layer is an alginic acid-coating layer (see prior art, page 8, lines 17-21, in particular).

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

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The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claims 1-5 rejected under 35 U.S.C. 103(a) as being unpatentable over Skjak-Braek et al [N] as applied to claims 1-4 above, and further in view of Huguet and Dellacherie [U].

Claim 1-5 are drawn to a carrier for cell culture comprising a water-containing polymer gel containing chitosan, which is coated with collagen and/or alginic acid, and comprises two or more coated layers; wherein an outermost layer is a collagen-coating layer or an alginic acid-coating layer; and wherein an outermost layer is an alginic acid coating layer; and which comprises a chitosan-coating layer as an outermost layer formed on an alginic acid-coating layer.

Prior art [N] teaches such a carrier in the form of microcapsules wherein the carrier is used to encapsulate cells, and is comprised of a hydrogel such as alginate and in addition contains chitosan in a multi-layer structure; wherein the outermost layer is an alginate-coating layer (see prior art [N], as discussed supra).

However, providing a chitosan-coating layer as an outermost layer formed on an alginic acid-coating layer as claimed in claim 5, and the use of such hydrogel membranes as a cell culture carrier, is not explicitly taught by the prior art [N].

Prior art [U] teaches a microcapsule comprising alginate beads that are coated with chitosan as an outermost layer (see prior art, abstract, methods, page 746, in particular) in order to study the rate of release of biological materials such as proteins and dextran (of different molecular weights) from the encapsulated beads.

It would have been obvious to the person of ordinary skill in the art at the time the invention was made to modify the microcapsules comprising water containing polymer gel containing chitosan, wherein the water containing polymer gel is coated with alginate such as taught by the prior art [N] in such a way that the support material comprises a chitosan-coating layer as an outermost layer formed on an alginic acid coating layer, as taught by prior art [U].

The person of ordinary skill in the art would have been motivated to make that modification because the prior art documents [U] discloses the benefits of using a coating of chitosan as an outermost layer in order to provide strength in terms of a reinforced gel layer, to limit the loss of encapsulated materials, and also to provide a method for the controlled release of the encapsulated biological materials (see prior art, abstract; page 745, first paragraph; page 150, last paragraph, in particular and references therein). In addition, the prior art [U] discloses the relationship between the rate of release of biological materials and the molecular weights, pH, net charge or ionization, specific conformations, etc. of the biological materials encapsulated within the alginate beads; and thus suggests albeit implicitly, the benefits of coating the beads with chitosan in order to control the movement of encapsulated biological materials (including cells, macromolecules, metabolic products, etc.).

Therefore, one of ordinary skill in the art would have had a reasonable expectation of success when modifying the microcapsules for encapsulating biological materials such as living cells as taught by the prior art [N] because the prior art [U] teaches the advantage of (having an outermost coating layer of chitosan on the alginate coating layer of the beads) such a modification for reinforcement and controlled release of encapsulated biological materials from such microcapsules.

The limitation "**for cell culture**" recited in claims 1-5 for a carrier provides an "intended use" for the carrier but does not confer any strict structural limitation on the carrier such as claimed (see MPEP § 2111.02 "[A] claim preamble has the import that the claim as a whole suggests for it." *Bell Communications Research, Inc. v. Vitalink Communications Corp.*, 55 F.3d 615, 620, 34 USPQ2d 1816, 1820 (Fed. Cir. 1995). "If the claim preamble, when read in the context of the entire claim, recites limitations of the claim, or, if the claim preamble is necessary to give life, meaning, and vitality' to the claim, then the claim preamble should be construed as if in the balance of the claim." *Pitney Bowes, Inc. v. Hewlett-Packard Co.*, 182 F.3d 1298, 1305, 51 USPQ2d 1161, 1165-66 (Fed. Cir. 1999). See also > *Jansen v. Rexall Sundown, Inc.*, 342 F.3d 1329, 1333, 68 USPQ2d 1154, 1158 (Fed. Cir. 2003)).

In addition, the proposed modification in the form of an outermost coating layer made of chitosan on an alginate gel layer as taught by prior art [U] does not render the invention of the prior art [N] unsuitable for its use in cell culture applications because the prior art [N] teaches the encapsulation of live cells which are in contact with the hydrogel materials and are in a condition suitable for biological materials (such as Islets

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of Langerhans for production of insulin) to be active for a prolonged period of time (see prior art [N], example 1-3, in particular) as needed for cell culture applications (see MPEP § 2143.01, "*If proposed modification would render the prior art invention being modified unsatisfactory for its intended purpose, then there is no suggestion or motivation to make the proposed modification. In re Gordon, 733 F.2d 900, 221 USPQ 1125 (Fed. Cir. 1984)*").

Therefore, it would have been obvious to a person of ordinary skill in the art at the time the invention was made to modify and use the invention of the prior art [N] as taught by prior art [U] as a carrier for cell culture such as claimed. One of ordinary skill in the art would have had a reasonable expectation of success in using the modified invention for cell culture purposes as the prior art [N] demonstrates the encapsulation of biological materials in a hydrogel containing chitosan that can be used for *in vivo* implantation and transplantation of biological materials including cells.

Thus the invention as a whole would have been *prima facie* obvious to one skill in the art at the time the invention was made.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Satyendra K. Singh whose telephone number is 571-272-8790. The examiner can normally be reached on 9-5MF.

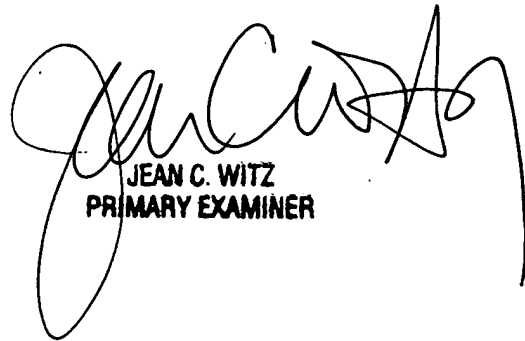
If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Wityshyn can be reached on 571-272-0926. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

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Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).



Satyendra K. Singh



JEAN C. WITZ
PRIMARY EXAMINER